SEQUENCE LISTING

<110> Leung, Shawn Shui-on

<120> REDUCING IMMUNOGENICITIES OF IMMUNOGLOBULINS BY FRAMEWORK-PATCHING

<130> 655

<140> US 09/892,613
<141> 2001-06-27

<160> 71

<170> PatentIn version 3.3

<210> 1
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> FR-patched heavy chaim variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 3 and 6) halves at the KpeI site.

<220>
<221> V_region
<222> (1)..(369)

<400> 1
gaagtgcagc tgctggagtc tgggggaggc ttagtgcagc ctggagggtc cctgaggctc 60

tcctgtgcag cctctggatt ctccttcagt atctatgaca tgtcttgggt tcgccaggca 120

ccgggaaagg ggctggagtg ggtcgcatac attagtagtg gtggtggtac cacctactat 180

ccagacactg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtac 240

ctgcaaatga acagtctgag ggtggaggac acagccttat attactgtgc aagacatagt 300

ggctacggta gtagctacgg ggttttgttt gcttactggg gccaagggac tctggtcact 360

gtctcttca 369

<210> 2
<211> 123
<212> PRT
<213> Chimaera sp.

<400> 2

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ile Tyr
20 25 30

Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 3
<211> 111
<212> DNA
<213> Artificial Sequence

<220>

<223> N-template is a synthetic sense-strand oligonucleotide encoding amino acide 14-50 of the VH region (SEQ ID No. 2). The template is PCR-amplified by two primers (SEQ ID No. 4 and 5)

<220>
<221> V_region
<222> (1)..(111)

<400> 3
cctggagggt ccctgaggct ctcctgtgca gcctctggat tctccttcag tatctatgac 60

atgtcttggg ttcgccaggc accgggaaag gggctggagt gggtcgcata c 111

<210> 4
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-19 of the VH region (SEQ ID No. 2). The 3' end of the primer overlaps with the 5'end of the template by 18 nucleotides.

<220>
<221> primer_bind
<222> (1)..(57)

<400> 4
gaagtgcagc tgctggagtc tgggggaggc ttagtgcagc ctggagggtc cctgagg 57

<210> 5
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 43-59 of the VH region(SEQ ID No. 2). The primer overlaps with the template by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(48)

<400> 5
gtaggtggta ccaccaccac tactaatgta tgcgacccac tccagccc 48

<210> 6
<211> 132
<212> DNA
<213> Artificial Sequence

<220>
<223> C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 68-111 of the VH region (SEQ ID No 2) The template is PCR-amplified by two primers (SEQ ID No 7 and 8)

<220>
<221> V_region
<222> (1)..(132)

<400> 6
ttcaccatct ccagagacaa tgccaagaac tccctgtacc tgcaaatgaa cagtctgagg 60

gtggaggaca cagccttata ttactgtgca agacatagtg gctacggtag tagctacggg 120

gttttgtttg ct 132

<210> 7
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 55-74 of the VH region (SEQ ID No 2). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(60)

<400> 7
ggtggtacca cctactatcc agacactgtg aagggccgat tcaccatctc cagagacaat 60

<210> 8
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 105-123 of the VH region (SEQ ID No 2). The primer and the template overlaps by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(57)

<400> 8
tgaagagaca gtgaccagag tcccttggcc ccagtaagca aacaaaaccc cgtagct 57

<210> 9
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> FR-patched light chaim variable region sequence formed by joining the N- and C- terminal (SEQ 11 and 14) halves at the KpeI site.

<220>
<221> V_region
<222> (1)..(321)

<400> 9
gatatccaga tgacccagtc tccatcctcc ctgtctgcct ctgtgggaga cagagtcacc 60

attagttgca gggcaagtca ggacattagc aattatttaa actggtatca gcagaaacca 120

ggtaaggctc cgaaactcct gatctactac actagtatat tacactcagg agtcccatca 180

aggttcagtg gcagtgggtc tggaacagaa tttactctca ccattagctc cctgcagcca 240

gaagattttg ccacttactt ttgccaacag ggtaatacgc ttccgtggac gttcggtgga 300

ggcaccaagg tggaaatcaa a 321

<210> 10
<211> 107
<212> PRT
<213> Chimaera sp.

<400> 10

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 11
<211> 108
<212> DNA
<213> Artificial Sequence

<220>
<223> N-template is a synthetic sense-strand oligonucleotide encoding amino acid 11-46 of the VL region (SEQ ID No. 10). The template is PCR-amplified by two primers (SEQ ID No. 12 and 13)

<220>
<221> V_region
<222> (1)..(108)

<400> 11
ctgtctgcct ctgtgggaga cagagtcacc attagttgca gggcaagtca ggacattagc 60

aattatttaa actggtatca gcagaaacca ggtaaggctc cgaaactc 108

<210> 12
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-17 of the VH region (SEQ ID No 10). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(51)

<400> 12
gatatccaga tgacccagtc tccatcctcc ctgtctgcct ctgtgggaga c 51

<210> 13
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 40-53. The primer and the template overlaps by 18 nucleotides.

<220>
<221> primer_bind
<222> (1)..(40)

<400> 13
atatactagt gtagtagatc aggagtttcg gagccttacc 40

<210> 14
<211> 120
<212> DNA
<213> Artificial Sequence

<220>
<223> C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 59-98 of the VH region (SEQ ID No 10) The template is PCR-amplified by tow primers (SEQ ID No 15 and 16)

<220>
<221> V_region
<222> (1)..(120)

<400> 14
ccatcaaggt tcagtggcag tgggtctgga acagaattta ctctcaccat tagctccctg 60

cagccagaag attttgccac ttacttttgc caacagggta atacgcttcc gtggacgttc 120

<210> 15
<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 50-65 of the VH region (SEQ ID No. 10). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides

<220>
<221> primer_bind
<222> (1)..(49)

<400> 15
ctacactagt atattacact caggagtccc atcaaggttc agtggcagt 49

<210> 16
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 92-107 of the VH region (SEQ ID No 10). The primer and the template overlaps by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(48)

<400> 16
tttgatttcc accttggtgc ctccaccgaa cgtccacgga agcgtatt 48

<210> 17
<211> 371
<212> DNA
<213> Artificial Sequence

<220>
<223> FR-patched heavy chaim variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 19 and 22) halves at the KpeI site.

<220>
<221> V_region
<222> (1)..(371)

<400> 17
caggtgcaac tggtggcttc cggggctgag gtaaataagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggcta cacatttacc agttacaata tgcactgggt acggcagcct 120

cctggaaggg gcctggaatg gattggagct atttatccag gaaatggtga tactagttac 180

aatcagaaat tcaagggcaa ggccacattg actgcagaca aatcctccag cacagcctac 240

atgcagctca gcagtctgac atctgaggac tctgcggtct attactgtgc aagatcgcac 300

tacggtagta actacgtaga ctactttgac tactggggcc aaggcaccac tgttacagtc 360

tcctctgatc a 371

<210> 18
<211> 123
<212> PRT
<213> Chimaera sp.

<400> 18

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Asp
115 120

<210> 19
<211> 114
<212> DNA
<213> Artificial Sequence

<220>
<223> N-template is a synthetic sense-strand oligonucleotide encoding amino acide 12-49 of the VH region (SEQ ID No. 18). The template is PCR-amplified by two primers (SEQ ID No. 20 and 21)

<220>
<221> V_region
<222> (1)..(114)

<400> 19
aataagcctg gggcctcagt gaaggtctcc tgcaaggctt ctggctacac atttaccagt 60

tacaatatgc actgggtacg gcagcctcct ggaaggggcc tggaatggat tgga 114

<210> 20
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-19 of the VH region (SEQ ID No 18). The 3' end of the primer overlaps with the 5'end of the template by 24 nucleotides.

<220>
<221> primer_bind
<222> (1)..(57)

<400> 20
caggtgcaac tggtggcttc cggggctgag gtaaataagc ctggggcctc agtgaag 57

<210> 21
<211> 55
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 43-60 of the VH region (SEQ ID No 18). The primer and the template overlaps by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(55)

<400> 21
tgtaactagt atcaccattt cctggataaa tagctccaat ccattccagg cccct 55

<210> 22
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<223> C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 70-111 of the VH region (SEQ ID No 18) The template is PCR-amplified by tow primers (SEQ ID No 23 and 24)

<220>
<221> V_region
<222> (1)..(126)

<400> 22
ttgactgcag acaaatcctc cagcacagcc tacatgcagc tcagcagtct gacatctgag 60

gactctgcgg tctattactg tgcaagatcg cactacggta gtaactacgt agactacttt 120

gactac 126

<210> 23
<211> 61
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 57-76 of the VH region (SEQ ID No 18). The 3' end of

the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(61)

<400> 23
tgatactagt tacaatcaga aattcaaggg caaggccaca ttgactgcag acaaatcctc 60

c 61

<210> 24
<211> 59
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 105-123 of the VH region (SEQ ID No 18). The primer and the template overlaps by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(59)

<400> 24
tgatcagagg agactgtaac agtggtgcct tggccccagt agtcaaagta gtctacgta 59

<210> 25
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> FR-patched light chaim variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 27 and 30) halves at the BspEI site.

<220>
<221> V_region

<222> (1)..(321)

<400> 25
gatattcaac tcacacagtc tccatcaagt ctttctgcat ctgtggggga cagagtcaca 60

attacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga 120

tcctccccca aaccctggat ttatgccaca tccaacctgg cttccggagt ccctagtcgc 180

ttcagtggca gtgggtctgg gaccgagttc actctcacaa tcagcagttt gcagcctgaa 240

gatttcgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300

accaagctga ccgttctacg g 321

<210> 26
<211> 107
<212> PRT
<213> Chimaera sp.

<400> 26

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg
100 105

<210> 27
<211> 129
<212> DNA
<213> Artificial Sequence

<220>
<223> N-template is a synthetic sense-strand oligonucleotide encoding amino acide 9-51 of the VL region (SEQ ID No. 26). The template is PCR-amplified by two primers (SEQ ID No. 28 and 29)

<220>
<221> V_region
<222> (1)..(129)

<400> 27
tcaagtcttt ctgcatctgt gggggacaga gtcacaatta cttgcagggc cagctcaagt 60

ttaagtttca tgcactggta ccagcagaag ccaggatcct cccccaaacc ctggatttat 120

gccacatcc 129

<210> 28
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-15 of the VH region (SEQ ID No 26). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(45)

<400> 28
gatattcaac tcacacagtc tccatcaagt ctttctgcat ctgtg 45

<210> 29
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 45-57. The primer and the template overlaps by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(40)

<400> 29
ggactccgga agccaggttg gatgtggcat aaatccaggg 40

<210> 30
<211> 120
<212> DNA
<213> Artificial Sequence

<220>
<223> C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 61-100 of the VH region (SEQ ID No 26) The template is PCR-amplified by tow primers (SEQ ID No 31 and 32)

<220>
<221> V_region
<222> (1)..(120)

<400> 30
ttcagtggca gtgggtctgg gaccgagttc actctcacaa tcagcagttt gcagcctgaa 60

gatttcgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 120

<210> 31
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 54-67 of the VH region (SEQ ID No 18). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(43)

<400> 31
ggcttccgga gtccctagtc gcttcagtgg cagtgggtct ggg 43

<210> 32
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 94-107 of the VH region (SEQ ID No 26). The primer and the template overlaps by 21 nucleotides.

<220>
<221> primer_bind
<222> (1)..(42)

<400> 32
ccgtagaacg gtcagcttgg tcccagcacc gaacgtgagc gg 42

<210> 33
<211> 123
<212> PRT
<213> Antibody

<400> 33

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

```
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ile Tyr
            20                  25                  30

Asp Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
        35                  40                  45

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala
        115                 120
```

<210> 34
<211> 107
<212> PRT
<213> Antibody

<400> 34

```
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1               5                   10                  15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45
```

```
Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 35
<211> 123
<212> PRT
<213> Immunoglobulin

<400> 35

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ile Tyr
            20                  25                  30

Asp Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
        35                  40                  45

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
```

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala
115 120

<210> 36
<211> 29
<212> PRT
<213> Immunoglobulin

<400> 36

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Pro Gly Gly Ser
1 5 10 15

Leu Arg Leu Ser Cys Ala Thr Thr Gly Phe Ala Phe Ser
20 25

<210> 37
<211> 30
<212> PRT
<213> Immunoglobulin

<400> 37

Gln Val Gln Leu Leu Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser
20 25 30

<210> 38
<211> 30
<212> PRT
<213> Immunoglobulin

<400> 38

```
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser
            20                  25                  30
```

<210> 39
<211> 14
<212> PRT
<213> Immunoglobulin

<400> 39

```
Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
1               5                   10
```

<210> 40
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 40

```
Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln
1               5                   10                  15


Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys Ala Arg
            20                  25                  30
```

<210> 41
<211> 11
<212> PRT
<213> Immunoglobulin

<400> 41

```
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Thr
1               5                   10
```

<210> 42
<211> 107
<212> PRT
<213> Immunoglobulin

<400> 42

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1   5   10   15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35   40   45

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65   70   75   80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 43
<211> 23
<212> PRT
<213> Immunoglobulin

<400> 43

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Ser Cys
            20

<210> 44
<211> 15
<212> PRT
<213> Immunglobulin

<400> 44

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
1   5   10   15

<210> 45
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 45

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1   5   10   15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys
            20   25   30

<210> 46
<211> 10
<212> PRT
<213> Immunoglobulin

<400> 46

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
1   5   10

<210> 47
<211> 123
<212> PRT
<213> Immunoglobulin

<400> 47

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ile Tyr
20 25 30

Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 48
<211> 107
<212> PRT
<213> Immunoglobulin

<400> 48

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr

```
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 49
<211> 123
<212> PRT
<213> Immunoglobulin

<400> 49

```
Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60
```

```
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80


Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Asp
        115                 120
```

<210> 50
<211> 107
<212> PRT
<213> Immunoglobulin

<400> 50

```
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1               5                   10                  15


Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20                  25                  30


His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
        35                  40                  45


Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50                  55                  60


Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65                  70                  75                  80


Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
                85                  90                  95
```

```
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg
            100                 105


<210>  51
<211>  123
<212>  PRT
<213>  Immunoglobulin

<400>  51

Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60


Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80


Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Asp
        115                 120


<210>  52
<211>  30
```

<212> PRT
<213> Immunoglobulin

<400> 52

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr
            20   25   30

<210> 53
<211> 14
<212> PRT
<213> Immunoglobulin

<400> 53

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly
1   5   10

<210> 54
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 54

Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
1   5   10   15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            20   25   30

<210> 55
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 55

```
Arg Ala Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Asn
1               5                   10                  15


Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Cys Cys Ala Arg
            20                  25                  30
```

<210> 56
<211> 11
<212> PRT
<213> Immunoglobulin

<400> 56

```
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1               5                   10
```

<210> 57
<211> 107
<212> PRT
<213> Immunoglobulin

<400> 57

```
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1               5                   10                  15


Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20                  25                  30


His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
        35                  40                  45


Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50                  55                  60


Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65                  70                  75                  80
```

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg
100 105

<210> 58
<211> 23
<212> PRT
<213> Immunglobulin

<400> 58

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys
20

<210> 59
<211> 22
<212> PRT
<213> Immunoglobulin

<400> 59

Asn Leu Met Leu Ile Gln Pro Pro Ser Val Ser Glu Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Met Thr Cys
20

<210> 60
<211> 15
<212> PRT
<213> Immunoglobulin

<400> 60

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Pro Val Ile Tyr

1 5 10 15

<210> 61
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 61

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys
20 25 30

<210> 62
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 62

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Thr Ser Leu Gln Pro Glu Asp Phe Ala Ala Tyr Phe Cys
20 25 30

<210> 63
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 63

Gly Val Pro Ser Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Phe
1 5 10 15

Leu Thr Ile Ser Ser Leu Arg Pro Glu Asp Val Ala Thr Tyr Phe Cys
20 25 30

<210> 64
<211> 32
<212> PRT
<213> Immunoglobulin

<400> 64

Gly Val Pro Ala Arg Phe Ser Gly Tyr Asn Ser Gly Asn Ser Ala Phe
1 5 10 15

Leu Thr Ile Asn Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Phe Cys
20 25 30

<210> 65
<211> 11
<212> PRT
<213> Immunoglobulin

<400> 65

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
1 5 10

<210> 66
<211> 11
<212> PRT
<213> Immunoglobulin

<400> 66

Phe Gly Val Gly Ser Lys Val Glu Ser Lys Arg
1 5 10

<210> 67
<211> 11
<212> PRT
<213> Immunoglobulin

<400> 67

```
Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg
1               5                   10
```

<210> 68
<211> 122
<212> PRT
<213> Immunoglobulin

<400> 68

```
Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 69
<211> 107
<212> PRT

<213> Immunoglobulin

<400> 69

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20   25   30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65   70   75   80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg
            100   105

<210> 70
<211> 122
<212> PRT
<213> Immunglobulin

<400> 70

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

```
Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 71
<211> 107
<212> PRT
<213> Immunoglobulin

<400> 71

```
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Pro Val Ile Tyr
        35                  40                  45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60
```

```
Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65                  70                  75                  80


Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
                85                  90                  95


Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg
            100                 105
```